

REMARKS

1. Status of the Application

Claims 1-13 are pending in the present application.

Claim 1 has been amended to describe particular embodiments of the invention, notwithstanding Applicant's belief that the unamended claim would have been allowable, without acquiescing to any of the Examiner's arguments, and without waiving the right to prosecute the unamended (or similar) claim in another application, but rather for the purpose of furthering Applicants' business goals and expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG).¹

In particular, Claim 1 has been amended to recite that "the quantity of the attached moiety that detaches from said surface when contacted with a solution comprising a concentration of arginine chosen from one or more concentrations in the range from 25 mM to 100 mM is higher than the quantity of the attached moiety that detaches from said surface when contacted with a solution comprising the same chosen concentration of cations chosen from one or more of sodium cations and magnesium cations." Support for this amendment is in the Specification, which shows the relative elution of two exemplary arginine tagged proteins when using a range of Na²⁺ concentrations (Figure 3) and Mg²⁺ concentrations (Figure 4A), as compared to arginine concentrations (Figure 4C).

Claim 4 has been amended to avoid language redundancy by cancelling the term "only."

Claim 6 has been amended by replacing "containing" with the term "comprising" in order to consistently use the same term in the claims.

Claims 8 and 9 have been amended by replacing the term "is" with "comprising" to describe one embodiment of the invention.

New Claims 56-91 have been added to better describe particular preferred embodiments of the invention.

Support for new Claims 56-57 and 83-84 is in Figure 4A which shows elution of two exemplary arginine tagged proteins using a range of Mg²⁺ concentrations.

¹ 65 Fed. Reg. 54603 (September 8, 2000).

Support for new Claims 58-59 and 85-86 is in Figure 3 which shows elution of two exemplary arginine tagged proteins using a range of Na^{2+} concentrations.

Support for new Claims 60 and 87 is in the Specification, page 22, lines 23-25, page 23, lines 6-8, and Figure 4B which shows elution of two exemplary arginine tagged proteins using a range of K^{+} concentrations.

Support for new Claims 61-62 and 88-89 is in the Specification, page 39, lines 18-20, and Figures 4B and 4C, which show the relative elution of two exemplary arginine tagged proteins when using a range of K^{2+} concentrations (Figure 4B) as compared to arginine concentrations (Figure 4C).

Support for new Claims 63-64 and 90-91 is in the Specification, page 22, lines 23-25, Figure 3, and Figure 4C, which show elution of two exemplary arginine tagged proteins when using a range of arginine concentrations.

Support for new Claims 65 and 81 is in the Specification, page 4, lines 20-21 and page 7, lines 13-15.

Support for new Claims 66, 67, and 82 is in the originally filed claims 2 and 4, and Specification, page 38, lines 26-28.

Support for new Claim 68 is in the Specification page 4, lines 17-20 and originally filed Claim 3.

New Claim 69 is supported by the Specification, page 8, lines 15-18.

Support for new Claim 70 is the same as discussed above for amended Claim 1.

Support for new Claims 71-80 is found in originally filed Claims 2-8 and 10-12.

New Claims 81-82 are supported by the same disclosure discussed above for Claims 65 and 67. New Claims 83-91 find the same support as for Claims 56-64.

These amendments do not introduce new matter.

2. Claim 13 is allowed, and dependent Claims 70-91 are in condition for allowance

Applicants note that "Claim 13 is allowed."² Applicants have added new Claims 70-91, which depend from Claim 13. In view of the above-discussed support for each of the

² Paper No. 16, item 15.

new claims, and since the new claims depend from an allowed claim, Applicants respectfully request allowance of new Claims 70-91.

3. Withdrawn Objections and Rejections

Applicants note, with appreciation, that the Examiner withdrew³ the following objections and rejections that were advanced in the prior office action:

- (a) Objection to the specification;
- (b) Rejection of Claim 6 and 7 under 35 USC 112, second paragraph, as allegedly indefinite;
- (c) Rejection of Claims 1 and 4-12 under 35 USC 103(a), as allegedly obvious over Hirabayashi *et al.* (1990) in view of Mueller *et al.*;
- (d) Rejection of Claims 1-12 under 35 USC 103(a), as allegedly obvious over Hirabayashi *et al.* (1992) in view of Mueller *et al.*;
- (e) Rejection of Claims 1-5, 8 and 9 under 35 USC 103(a) over Mueller *et al.* in view of Hirabayashi *et al.* (1992);
- (f) Rejection of Claims 1-12 under 35 USC 103(a) over Sassenfeld *et al.* in view of Geke *et al.*; and
- (g) Objection to Claim 13 as depending from a rejected claim.

4. New Rejection of Claims 1-12 under 35 U.S.C. §103(a) over Sassenfeld *et al.* in view of Suzuki *et al.* and Pinnavaia *et al.*

Claims 1-12 stand rejected under 35 U.S.C. §103(a) over Sassenfeld *et al.* in view of Suzuki *et al.* (U.S. Patent No. 4,629,713) and Pinnavaia *et al.* (U.S. Patent No. 5,993,769).⁴ Applicants respectfully disagree, because a *prima facie* case of obviousness is not established.

A *prima facie* case of obviousness requires the Examiner to cite to a combination of references which (a) suggests or motivates one of skill in the art to combine the claim elements to yield the claimed combination, (b) discloses all the elements of the claimed invention, **and** (c) provides a reasonable expectation of success should the claimed

³ Paper No. 16, pages 2 and 3.

⁴ Paper No. 16, page 4, item 13.

combination be carried out. Failure to establish **any one** of these three requirements precludes a finding of a *prima facie* case and, without more, entitles Applicants to withdrawal of the rejection based on obviousness.⁵ None of these 3 necessary requirements has been established.

i. The References Fail to Disclose All The Claims' Limitations

It is axiomatic for establishing a *prima facie* case of obviousness that "all the claim limitations must be taught or suggested by the prior art."⁶ This has not been done.

Sassenfeld *et al.* discloses purification of urogastrone, which is fused to five arginines at its carboxyl terminus, on SP-Sephadex. Suzuki *et al.* discloses "cation exchanged layered silicates"⁷ such as "montmorillonite, hectorite, saponite, nontronite, beidellite, fluorohectorite, and laponite, and mixed layered 2:1 silicates such as rectorite, synthetic mica montmorillonite, and illite and vermiculite and mica-like compositions containing up to 2.0 e³¹ /O₂₀ unit cell such as muscovite, biotite, phlogopite, synthetic mica montmorillonite, taeniolite, and tetrasilicic mica."⁸ Pinnavaia *et al.* discloses that "Montmorillonite, therefore, possesses abundant cation-exchange ability."⁹

It is notable, however, that none of the references discloses that contacting the arginine residues of Sassenfeld *et al.* with the surface of the silicates of either Suzuki *et al.* or Pinnavaia *et al.* results in attachment of Sassenfeld *et al.*'s urogastrone to the surface of the silicate, "wherein the quantity of the attached moiety that detaches from said surface when contacted with a solution comprising a concentration of arginine chosen from one or more concentrations in the range from 25 mM to 100 mM is higher than the quantity of the attached moiety that detaches from said surface when contacted with a solution comprising the

⁵ MPEP §2143; *See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

⁶ MPEP 2143.03, citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

⁷ Suzuki *et al.* column, 1, lines 31-35; and Table 1.

⁸ Suzuki *et al.*, column 23, lines 4-14.

⁹ Pinnavaia *et al.*, column 1, lines 25-26.

same chosen concentration of cations chosen from one or more of sodium cations and magnesium cations," as recited by Claims 1-12 (and new claims 56-70).

In view of the deficiency of this prong, a *prima facie* case cannot stand with respect to any of the pending claims.

ii. Motivation To Combine the Elements Is Lacking

A key requirement for a *prima facie* case of obviousness is whether a person skilled in the art would be **motivated** to modify the reference to arrive at the **claimed invention**.¹⁰ In particular,

"the examiner must show *reasons* that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would *select* the elements from the cited prior art references for *combination in the manner claimed*."¹¹ To find a claim obvious, there must be "a reason or suggestion (explicit or implicit) in the art for combining the art as proposed."¹² Evidence of a suggestion, teaching, or motivation to modify prior art references "must be *clear and particular*."¹³ The Patent Office "... cannot rely on conclusory statements when dealing with particular combinations of prior art and specific claims, but *must set forth the rationale* on which it relies."¹⁴

At the outset, the Examiner is respectfully reminded that the claimed invention relates to the recited **combination** of parameters, namely attaching an arginine tagged moiety to layered silicate.

¹⁰ *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988) and *In re Jones*, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992).

¹¹ (Emphasis added) *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998); *See, also, Robotic Vision Systems Inc. v. View Engineering Inc.*, 51 USPQ2d 1948 (Fed. Cir. 1999); *Sibia Neurosciences v. Cadus Pharmaceutical Corp.*, 225 F.3d 1349, 1355-56 (Fed. Cir. 2000); *In re Oetiker*, 977 F.2d 1443, 1448 (Fed. Cir. 1992).

¹² *Sibia Neurosciences v. Cadus Pharmaceutical Corp.*, 225 F.3d 1349, 1355-56 (Fed. Cir. 2000); *In re Oetiker*, 977 F.2d 1443, 1448 (Fed. Cir. 1992).

¹³ (Emphasis added) *In re Dembiczak*, 175 F.3d 994, 50 USPQ2d 1614 (Fed. Cir. 1999), *citing C.R. Bard*, 157 F.3d 1340 at 1352, 48 USPQ2d at 1232. *See, also, In re Sang Su Lee*, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002).

¹⁴ (Emphasis added).

The Examiner **admitted** that "Sassenfeld *et al.* do **not** teach the use of a layered silicate substrate or mica in their method."¹⁵ To bridge this gap, the Examiner argued that "one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of cost effectiveness, since Pinnavaia *et al.* explicitly taught that layered inorganic ion exchangers are highly preferred due to their advantageous low cost and broad range of particle sizes."¹⁶ Importantly, however, there was no teaching or suggestion in the references, alone or in combination, with regard to the **differential ability** of sodium ions and/or magnesium ions to elute moieties that are attached to layered silicate surfaces, as compared to elution with arginine. This surprising discovery was **first** made by the instant inventors. To underscore this discovery, Applicants have amended Claim 1¹⁷ to recite that "the quantity of the attached moiety that detaches from said surface when contacted with a solution comprising a concentration of arginine chosen from one or more concentrations in the range from 25 mM to 100 mM is higher than the quantity of the attached moiety that detaches from said surface when contacted with a solution comprising the same chosen concentration of cations chosen from one or more of sodium cations and magnesium cations." Since the art **did not know** of the recited preferential elution of arginine tagged moieties in the presence of arginine *vis a vis* the presence of magnesium and/or sodium cations, there can be no motivation to combine the references. This precludes a *prima facie* case of obviousness.¹⁸

¹⁵ Paper No. 16, page 4, last full paragraph.

¹⁶ Paper No. 16, page 5, second full paragraph. Applicants believe that the Examiner intended to refer to Suzuki *et al.* rather than Pinnavaia *et al.*, since Suzuki *et al.*, column 23, lines 15-18, discloses "The broad range of particle sizes, ion exchange capacities and the low cost of these layered inorganic ion exchangers are highly preferred."

¹⁷ Claim 1 has been amended to describe particular embodiments of the invention, notwithstanding Applicant's belief that the unamended claim would have been allowable, without acquiescing to any of the Examiner's arguments, and without waiving the right to prosecute the unamended (or similar) claim in another application, but rather for the purpose of furthering Applicants' business goals and expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG).

¹⁸ Applicants also note that new Claims 60-62 are non-obvious for the additional reason that the art **did not know** of the recited preferential elution of arginine tagged moieties

iii. A Reasonable Expectation Of Success Is Not Established

A fundamental requisite of establishing a *prima facie* case of obviousness is that there is a reasonable expectation of success in practicing the invention.

"[T]he reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure."¹⁹

The Examiner argued that it would have been obvious "to replace Sassenfeld's cation exchange resin material with Suzuki's layered silicate cation-exchange material, such as, mica or montmorillonite, to produce the instant invention with a reasonable expectation of success ... [because this] would have been well within the realm of routine experimentation and would have brought about similar results."²⁰ This argument suffers from at least two problems.

First, routine experimentation does not equate with obviousness. The court has expressly stated that:

"[W]e do not agree that 'routine experimentation' negatives patentability. The last sentence of section 103 states that 'patentability shall not be negated by the manner in which the invention was made.'²¹

Thus, the Examiner's argument improperly overlooks the express words of 35 USC § 103.

Second, the Examiner has **not provided evidence** to support his contention that substituting Sassenfeld *et al.*'s cation exchange Sephadex with Suzuki *et al.*'s layered silicate cation exchange material "would have brought about similar results." Indeed, such evidence **cannot** be advanced, since it was the inventors, not the prior art, who **first discovered the differential ability** of sodium ions and/or magnesium ions to elute moieties that are attached to layered silicate surfaces, as compared to elution with arginine.

For these reasons, a reasonable expectation in practicing the claimed combination is absent.

in the presence of arginine as compared to potassium cations.

¹⁹ *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) as cited in *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

²⁰ Paper No. 16, page 5, second full paragraph.

²¹ *In re Fay and Fox*, 146 USPQ 47, 51 (CCPA 1965).

Because not just one, but all three elements of a *prima facie* case of obviousness are not established, Applicants respectfully request the Examiner to withdraw the rejection based on alleged obviousness.

5. Additional Art of Record

Applicants note that the Examiner cited the following art that was "**not** relied upon in any of the rejections:"²² Keeling *et al.* 6,107,060, filed 09/30/1996); Brewer *et al.* (U.S. Patent No. 4,880,911); Konnecke *et al.* (1982); Sugimori *et al.* (JP 356152741); Charych (U.S. Patent No. 6,468,759); Xu *et al.* (U.S. Patent No. 5,874,668); Lloyd *et al.* (U.S. Patent No. 5,177,005); Kasakabe *et al.* (U.S. Patent No. 4,614,714); Elahi (U.S. Patent No. 4,338,094); Gaafar (U.S. Patent No. 4,029,756); Brizzard (U.S. Patent No. 6,379,903); Dorval (U.S. Patent No. 5,561,045); Neurath *et al.* (U.S. Patent No. 5,230,998); and Suzuki *et al.* (U.S. Patent No. 4,629,713).

CONCLUSION

All grounds of rejection and objection of the Office Action of July 15, 2003 having been addressed, reconsideration of the application is respectfully requested. To expedite prosecution, Applicants respectfully request the Examiner to **call the undersigned at (415) 904-6500 before drafting another written communication**, if any.

Signed on behalf of:

Dated: October 15, 2003



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²² (Emphasis added) Paper No. 16, page 5, item 14.